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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,074	10/28/2005	Kazuhisa Sugimura	64395(70904)	3084

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EXAMINER	
JIANG, DONG	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,074	SUGIMURA ET AL.	
	Examiner	Art Unit	
	DONG JIANG	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-14,16,25-27,29 and 31-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3* is/are allowed.

6)☒ Claim(s) *7-14,16,25-27,29 and 31-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 20 December 2007 is acknowledged and entered. Following the amendment, claims 4-6, 15, 18, 20, 21 and 30 are canceled, claims 1-3, 7, 8, 12-14, 16, 27 and 29 are amended, and the new claims 31-43 are added.

Currently, claims 1-3, 7-14, 16, 25-27, 29 and 31-43 are pending and under consideration.

Note, the status identifier of claims 17 and 28 indicates "previously presented", which is incorrect because the claims had been canceled (see amendment filed on 7/24/07). The correct status identifier for claims 17 and 28 should be "canceled".

Withdrawal of Objections and Rejections:

All objections and rejections of claims 4-6, 15, 18, 20, 21 and 30 are moot as the applicant has canceled the claims.

The objection of claims 7, 14 and 16 is withdrawn in view of applicant's amendment.

The rejection of claims 1-3, 7-10, 12, 16, 25, 26 and 29 under 35 U.S.C. 101, for being directed to non-statutory subject matter is withdrawn view of applicant's amendment.

The rejection of claims 3, 8, 14, 25-27 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment and argument.

The prior art rejection of claims 7, 9-11 and 14 under 35 U.S.C. 102(b) as being anticipated by Ghayur et al. (WO 01/589565) is withdrawn in view of applicant's amendment.

Formal Matters:

Claims

Claims 12, 33 and 34 are objected to for the following informalities, appropriate correction is required for each item:

Claim 12 recites "the detector using *either (1)* …", however, there is only one item ("(1)") recited in the claim. "The detector *comprising* antibody according to …" is suggested.

Claims 33 and 34 recite "wherein the antibody comprises:" in lines 3-4, which should be omitted because it is redundant.

Further, applicant is advised that should claim 33 be found allowable, claim 42 will be objected to; and that should claim 34 be found allowable, claim 43 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 10 remains rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim recites "[A] transformant", which, according to the specification, embraces not only cells, tissues, and organs but also individual animals (page 25, 1st paragraph), and reads on host cells intended for gene therapy. The specification teaches that the gene of the present invention can be used as a gene therapy agent for human-IL-18-related disease (page 20, lines 7-9 from the bottom). The scope of the claim, therefore, encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation "An isolated host cell" would be remedial. See 1077 O.G. 24, April 21, 1987.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-14, 16, 27 and 29 remain rejected, and the new claims 35, 37 and 40-43 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 remains indefinite because it is incomplete. The preamble recites "a method for diagnosing immunological disease", however, it is unclear how to achieve such, for example, what is indicative of the disease (*increased* IL-18?), or based on what a diagnosis can be made. Claims 33, 34, 42 and 43 are similarly indefinite.

Claim 27 remains rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the method steps of the process, i.e., how to *cause* a host to express the gene, is the host a cell or an animal transfected with said gene, or the host naturally carries the gene?

Applicants argument filed on 20 December 2007 has been fully considered, but is not deemed persuasive for the reasons below.

At page 9 of the response, the applicant argues that the specification entitled "A Recombinant Expression Vector and the Like of the Present Invention" where a genetic engineering technique is taught that would result in a host expressing a gene of interest, and these techniques were routinely preformed by those of skill in the art at the time of filing the instant application. This argument is not persuasive because the issue is not whether the specification teaches or the prior has established the genetic engineering technique, the issue is that the claim, as written, is incomplete because it misses method steps as to how to *cause* a host can express the gene. The claim depends from claim 8, which is directed to a gene, not a host cell containing the transfected gene or the vector thereof. Thus, it is unclear how to cause a host to express the gene.

Claim 37 is indefinite for the recitation "one or more amino acids of *at least one of the polypeptides* ..." because there is only one polypeptide recited (line 2) (and the other one is "peptide", in line 5).

The remaining claims are included in this rejection because they are dependent from the specifically mentioned claims without resolving the indefiniteness issue belonging thereto.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-13, 16, 25-27, 29, 31, 32, 36-39, 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to claims 7-11, 25-27, 31, 32 and 36, they are directed to or encompass a "gene" encoding a human antibody. In general, the term "gene" would necessarily mean a strand of DNA containing a promoter, and coding and non-coding sequence, which can regulate gene expression. However, the specification merely discloses the coding regions ("cDNA", see page 7, lines 9-10 of paragraph under "Disclosure of invention", for example) of the antibody polypeptides, i.e., SEQ ID NO:1 and 7, and no other DNA sequence (such as a promoter sequence) is identified or particularly described.

With respect to claims 37-39 and their dependent claims 12, 13, 16, 29, 40 and 41, they are directed to or encompass variants of the human antibody, having one *or more* amino acids substituted, deleted, inserted and/or added in the defined polypeptides (claims 37-39, for example), which read on *functional equivalents* of the antibody polypeptides of the recited SEQ ID NOs as there is no clear limitation as to how many amino acids can be substituted or modified. Thus, the claims encompass significant structural dissimilarity as compared to the disclosed antibody polypeptides of SEQ ID NO:3 and 9, including functional equivalents without any sequence similarity to the disclosed SEQ ID NO:3 and 9. However, the specification discloses the amino acid sequences with particularity for *one* human anti-hIL-18 antibody, namely, SEQ ID NO:3 (VH) and SEQ ID NO:9 (VL), and no variant of the human IL-18 antibody with amino acid substitution, insertion, addition, deletion, or any other type of "functional equivalents" meeting the limitations of these claims were ever identified or particularly described.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making

the claimed product, or any combination thereof. In this case, with respect to claims 37-39 and their dependent claims 12, 13, 16, 29, 40 and 41, the only factor present in the claims is functional characteristic, binding hIL-18 and inhibiting its activity. There is no sequence similarity required for the claimed variants. As such, with the exception of SEQ ID NO:3 and 9, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants, therefore, conception is not achieved regardless of the complexity or simplicity of the method of making a variant polypeptide. With respect to claims 7-11, 25-27, 31, 32 and 36, none of the factors is present as the specification does not provide any "gene" encoding said antibody polypeptides (replace "gene" with "cDNA" would be remedial). Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, no "gene" meets the written description provision of 35 U.S.C. §112, first paragraph; and only the antibody polypeptides of SEQ ID NO:3 and 9, but not the full breadth of the claims (variants with "one or more amino acids" substituted, deleted, inserted and/or added) meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

Claim interpretation: claims 37-39 and their dependent claims 12, 13, 16, 29, 40 and 41, are directed to or encompass variants of the human antibody, having one *or more* amino acids substituted, deleted, inserted and/or added in the defined polypeptides (claims 37-39, for example), which read on *functional equivalents* of the antibody polypeptides of the recited SEQ ID NOs as there is no limitation as to how many amino acids can be substituted or modified (i.e., the entire sequences could be changed so long as the polypeptides remain the functional activity). Therefore, any polypeptide with the recited functional property would read on such variants.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-39 and their dependent claims 12, 16, 29, 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Ghayur et al. (WO 01/589565 A2, Aug. 16, 2001, provided by applicants), for the reasons addressed in the rejection of claims 5-7, 9-12, 14-16, 18, 20, 21 and 29 by the same reference, set forth in the last Office Action mailed on 9/20/07, at pages 6-7, and for the reasons below.

The teachings of Ghayur were reviewed in the last Office Action, and are reiterated herein:

Ghayur discloses antibodies to human IL-18, and pharmaceutical compositions thereof, wherein the antibodies are entirely human antibodies, have high affinity for hIL-18 and neutralize hIL-18 activity, and are useful for detecting hIL-18 and for inhibiting hIL-18 activity in a human subject suffering from a disorder in which hIL-18 activity is detrimental, such as diseases involving immune and inflammatory elements (abstract, page 4, lines 12-16, and page 22, lines 26-28). Additionally, Ghayur teaches that an antibody may be part of a larger immunoadhesion molecules including use of a marker peptide and a C-terminal poly-His tag (page 17, lines 3-9). Further, Ghayur teaches a method for detecting hIL-18 in a biological

sample with said antibody (page 33, lines 6-10), and that a disorder in which hIL-18 activity is detrimental may be evidenced by an increase in the concentration of IL-18 in a biological fluid of a subject suffering from the disorder, which can be detected using said anti-IL-18 antibody (page 35, lines 7-11), indicating a method of diagnosis using the antibody.

The present claims 37-39, as written, read on functional equivalents of the disclosed antibody polypeptides because there is no limitation as to how many amino acids can be substituted or modified in the claims, therefore, there is no structural limitation for the claimed antibody variants. As such, Ghayur's IL-18 antibody meets the claim limitation as such a functional equivalent. Therefore, the reference anticipates the present claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 13 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Ghayur et al. (WO 01/589565 A2), as applied to claims 37-39 and claims 12, 16, 29, 40 and 41 above, for the reasons of record set forth in the last Office Action mailed 9/20/07, at pages 7-8, and for the reasons above.

Conclusion:

Claims 1-3 are allowable.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dong Jiang/
Primary Examiner, Art Unit 1646
3/30/08